

## SEQUENCE LISTING

<110> APPLIED RESEARCH SYSTEMS ARS HOLDING N.V.

<120> USE OF PRION CONVERSION MODULATING AGENTS

<130> WO/845

<160> 3

<170> PatentIn version 3.1

<210> 1

<211> 4563

<212> PRT

<213> Homo sapiens

<400> 1

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Leu Arg Lys Tyr Thr Tyr Asn Tyr Glu Ala Glu Ser Ser Ser Gly Val  
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Pro Gly Thr Ala Asp Ser Arg Ser Ala Thr Arg Ile Asn Cys Lys Val  
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Glu Leu Glu Val Pro Gln Leu Cys Ser Phe Ile Leu Lys Thr Ser Gln  
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Cys Thr Leu Lys Glu Val Tyr Gly Phe Asn Pro Glu Gly Lys Ala Leu  
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Leu Lys Lys Thr Lys Asn Ser Glu Glu Phe Ala Ala Ala Met Ser Arg  
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Tyr Glu Leu Lys Leu Ala Ile Pro Glu Gly Lys Gln Val Phe Leu Tyr  
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Pro Glu Lys Asp Glu Pro Thr Tyr Ile Leu Asn Ile Lys Arg Gly Ile  
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Ile Ser Ala Leu Leu Val Pro Pro Glu Thr Glu Glu Ala Lys Gln Val

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Leu Phe Leu Asp Thr Val Tyr Gly Asn Cys Ser Thr His Phe Thr Val  
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Lys Thr Arg Lys Gly Asn Val Ala Thr Glu Ile Ser Thr Glu Arg Asp  
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Leu Gly Gln Cys Asp Arg Phe Lys Pro Ile Arg Thr Gly Ile Ser Pro  
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Leu Ala Leu Ile Lys Gly Met Thr Arg Pro Leu Ser Thr Leu Ile Ser  
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Ser Ser Gln Ser Cys Gln Tyr Thr Leu Asp Ala Lys Arg Lys His Val  
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Glu Asp Thr Pro Lys Ile Asn Ser Arg Phe Phe Gly Glu Gly Thr Lys  
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Ala Arg Asp Gln Arg Ser Arg Ala Thr Leu Tyr Ala Leu Ser His Ala  
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Pro Thr Val Met Asp Phe Arg Lys Phe Ser Arg Asn Tyr Gln Leu Tyr  
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Glu Ile Gly Leu Glu Gly Lys Gly Phe Glu Pro Thr Leu Glu Ala Leu  
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Trp Val Asn Gly Gln Val Pro Asp Gly Val Ser Lys Val Leu Val Asp  
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His Phe Gly Tyr Thr Lys Asp Asp Lys His Glu Gln Asp Met Val As n  
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Gly Ile Met Leu Ser Val Glu Lys Leu Ile Lys Asp Leu Lys Ser Lys  
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Ser Ser Ser Gly Val Ile Ala Pro Gly Ala Lys Ala Gly Val Lys Leu  
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Glu Val Ala Asn Met Gln Ala Glu Leu Val Ala Lys Pro Ser Val Ser  
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Val Glu Phe Val Thr Asn Met Gly Ile Ile Ile Pro Asp Phe Ala Arg  
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Ser Gly Val Gln Met Asn Thr Asn Phe Phe His Glu Ser Gly Leu Glu  
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Pro Lys Arg Pro Val Lys Leu Leu Ser Gly Gly Asn Thr Leu His Leu  
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Val Ser Thr Thr Lys Thr Glu Val Ile Pro Pro Leu Ile Glu Asn Arg  
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995 1000 1005

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Met Ser Ser Trp Leu Gln Lys Ala Ser Gly Ser Leu Pro Tyr Thr  
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Gly Ser Tyr Ala Glu Met Lys Phe Asp His Thr Asn Ser Leu Asn  
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Tyr Ser Ser Asp Lys Phe Tyr Lys Gln Thr Val Asn Leu Gln Leu  
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Gln Pro Tyr Ser Leu Val Thr Thr Leu Asn Ser Asp Leu Lys Tyr  
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Asn Glu Ile Lys His Ile Tyr Ala Ile Ser Ser Ala Ala Leu Ser  
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Ala Phe Thr Phe Ser His Asp Tyr Lys Gly Ser Thr Ser His His  
1940 1945 1950

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1955 1960 1965

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1985 1990 1995

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2000 2005 2010

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2015 2020 2025

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2050

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Val Tyr Leu Glu Ser Leu Gln Asp Thr Lys Ile Thr Leu Ile Ile  
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Val Gly Gln Val Tyr Ser Thr Leu Val Thr Tyr Ile Ser Asp Trp  
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Trp Thr Leu Ala Ala Lys Asn Leu Thr Asp Phe Ala Glu Gln Tyr  
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Ser Ile Gln Asp Trp Ala Lys Arg Met Lys Ala Leu Val Glu Gln  
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Val Gln Ile Asn Phe Lys Asp Leu Lys Asn Ile Lys Ile Pro Ser  
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Pro Asp Leu His Ile Pro Glu Phe Gln Leu Pro His Ile Ser His  
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His Gly Ser Glu Met Leu Phe Phe Gly Asn Ala Ile Glu Gly Lys  
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Ser Asn Thr Val Ala Ser Leu His Thr Glu Lys Asn Thr Leu Glu  
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Asp Ser Asn Thr Lys Tyr Phe His Lys Leu Asn Ile Pro Lys Leu  
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Asp Phe Ser Ser Gln Ala Asp Leu Arg Asn Glu Ile Lys Thr Leu  
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Trp Lys Trp Ala Cys Pro Arg Phe Ser Asp Glu Gly Thr His Glu  
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Ser Gln Ile Ser Phe Thr Ile Glu Gly Pro Leu Thr Ser Phe Gly  
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Ser Thr Asn Asn Glu Gly Asn Leu Lys Val Arg Phe Pro Leu Arg  
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Leu Thr Gly Lys Ile Asp Phe Leu Asn Asn Tyr Ala Leu Phe Leu  
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Tyr Thr Ile Ile Thr Thr Pro Pro Leu Lys Asp Phe Ser Leu Trp  
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Glu Lys Thr Gly Leu Lys Glu Phe Leu Lys Thr Thr Lys Gln Ser  
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Arg Thr Phe Gln Ile Pro Gly Tyr Thr Val Pro Val Val Asn Val  
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Glu Val Ser Pro Phe Thr Ile Glu Met Ser Ala Phe Gly Tyr Val  
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Asp Val Arg Val Pro Ser Tyr Thr Leu Ile Leu Pro Ser Leu Glu  
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Leu Pro Val Leu His Val Pro Arg Asn Leu Lys Leu Ser Leu Pro  
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His Phe Lys Glu Leu Cys Thr Ile Ser His Ile Phe Ile Pro Ala  
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Met Gly Asn Ile Thr Tyr Asp Phe Ser Phe Lys Ser Ser Val Ile  
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Tyr Lys Leu Glu Gly Thr Thr Arg Leu Thr Arg Lys Arg Gly Leu  
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Glu Gly Leu Phe Phe Thr Asn Gly Glu His Thr Ser Lys Ala Thr  
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Leu Glu Leu Ser Pro Trp Gln Met Ser Ala Leu Val Gln Val His  
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Ala Ser Gln Pro Ser Ser Phe His Asp Phe Pro Asp Leu Gly Gln  
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Lys Asn Glu Val Arg Ile His Ser Gly Ser Phe Gln Ser Gln Val  
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Glu Leu Ser Asn Asp Gln Glu Lys Ala His Leu Asp Ile Ala Gly  
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Val Tyr Asp Lys Ser Leu Trp Asp Phe Leu Lys Leu Asp Val Thr  
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Val Tyr Thr Lys Asn Pro Asn Gly Tyr Ser Phe Ser Ile Pro Val  
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Thr Asp Leu Gln Val Pro Ser Cys Lys Leu Asp Phe Arg Glu Ile  
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Gly Ile Val Ile Pro Ser Phe Gln Ala Leu Thr Ala Arg Phe Glu

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Ser Thr Val Gln Phe Leu Glu Tyr Glu Leu Asn Val Leu Gly Thr  
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His Lys Ile Glu Asp Gly Thr Leu Ala Ser Lys Thr Lys Gly Thr  
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Leu Ala His Arg Asp Phe Ser Ala Glu Tyr Glu Glu Asp Gly Lys  
3950 3955 3960

Phe Glu Gly Leu Gln Glu Trp Glu Gly Lys Ala His Leu Asn Ile  
3965 3970 3975

Lys Ser Pro Ala Phe Thr Asp Leu His Leu Arg Tyr Gln Lys Asp  
3980 3985 3990

Lys Lys Gly Ile Ser Thr Ser Ala Ala Ser Pro Ala Val Gly Thr  
3995 4000 4005

Val Gly Met Asp Met Asp Glu Asp Asp Asp Phe Ser Lys Trp Asn  
4010 4015 4020

Phe Tyr Tyr Ser Pro Gln Ser Ser Pro Asp Lys Lys Leu Thr Ile  
4025 4030 4035

Phe Lys Thr Glu Leu Arg Val Arg Glu Ser Asp Glu Glu Thr Gln  
4040 4045 4050

Ile Lys Val Asn Trp Glu Glu Glu Ala Ala Ser Gly Leu Leu Thr  
4055 4060 4065

Ser Leu Lys Asp Asn Val Pro Lys Ala Thr Gly Val Leu Tyr Asp  
4070 4075 4080

Tyr Val Asn Lys Tyr His Trp Glu His Thr Gly Leu Thr Leu Arg  
4085 4090 4095

Glu Val Ser Ser Lys Leu Arg Arg Asn Leu Gln Asn Asn Ala Glu  
4100 4105 4110

Trp Val Tyr Gln Gly Ala Ile Arg Gln Ile Asp Asp Ile Asp Val  
4115 4120 4125

Arg Phe Gln Lys Ala Ala Ser Gly Thr Thr Gly Thr Tyr Gln Glu  
4130 4135 4140

Trp Lys Asp Lys Ala Gln Asn Leu Tyr Gln Glu Leu Leu Thr Gln  
4145 4150 4155

Glu Gly Gln Ala Ser Phe Gln Gly Leu Lys Asp Asn Val Phe Asp  
4160 4165 4170

Gly Leu Val Arg Val Thr Gln Lys Phe His Met Lys Val Lys His  
4175 4180 4185

Leu Ile Asp Ser Leu Ile Asp Phe Leu Asn Phe Pro Arg Phe Gln  
4190 4195 4200

Phe Pro Gly Lys Pro Gly Ile Tyr Thr Arg Glu Glu Leu Cys Thr  
4205 4210 4215

Met Phe Ile Arg Glu Val Gly Thr Val Leu Ser Gln Val Tyr Ser  
4220 4225 4230

Lys Val His Asn Gly Ser Glu Ile Leu Phe Ser Tyr Phe Gln Asp  
4235 4240 4245

Leu Val Ile Thr Leu Pro Phe Glu Leu Arg Lys His Lys Leu Ile  
4250 4255 4260

Asp Val Ile Ser Met Tyr Arg Glu Leu Leu Lys Asp Leu Ser Lys  
4265 4270 4275

Glu Ala Gln Glu Val Phe Lys Ala Ile Gln Ser Leu Lys Thr Thr  
4280 4285 4290

Glu Val Leu Arg Asn Leu Gln Asp Leu Leu Gln Phe Ile Phe Gln  
4295 4300 4305

Leu Ile Glu Asp Asn Ile Lys Gln Leu Lys Glu Met Lys Phe Thr  
4310 4315 4320

Tyr Leu Ile Asn Tyr Ile Gln Asp Glu Ile Asn Thr Ile Phe A sn  
4325 4330 4335

Asp Tyr Ile Pro Tyr Val Phe Lys Leu Leu Lys Glu Asn Leu Cys  
4340 4345 4350

Leu Asn Leu His Lys Phe Asn Glu Phe Ile Gln Asn Glu Leu Gln  
4355 4360 4365

Glu Ala Ser Gln Glu Leu Gln Gln Ile His Gln Tyr Ile Met Ala  
4370 4375 4380

Leu Arg Glu Glu Tyr Phe Asp Pro Ser Ile Val Gly Trp Thr Val  
4385 4390 4395

Lys Tyr Tyr Glu Leu Glu Glu Lys Ile Val Ser Leu Ile Lys Asn  
4400 4405 4410

Leu Leu Val Ala Leu Lys Asp Phe His Ser Glu Tyr Ile Val Ser  
4415 4420 4425

Ala Ser Asn Phe Thr Ser Gln Leu Ser Ser Gln Val Glu Gln Phe  
4430 4435 4440

Leu His Arg Asn Ile Gln Glu Tyr Leu Ser Ile Leu Thr Asp Pro  
4445 4450 4455

Asp Gly Lys Gly Lys Glu Lys Ile Ala Glu Leu Ser Ala Thr Ala  
4460 4465 4470

Gln Glu Ile Ile Lys Ser Gln Ala Ile Ala Thr Lys Lys Ile Ile  
4475 4480 4485

Ser Asp Tyr His Gln Gln Phe Arg Tyr Lys Leu Gln Asp Phe Ser  
4490 4495 4500

Asp Gln Leu Ser Asp Tyr Tyr Glu Lys Phe Ile Ala Glu Ser Lys  
4505 4510 4515

Arg Leu Ile Asp Leu Ser Ile Gln Asn Tyr His Thr Phe Leu Ile  
4520 4525 4530

Tyr Ile Thr Glu Leu Leu Lys Lys Leu Gln Ser Thr Thr Val Met  
4535 4540 4545

Asn Pro Tyr Met Lys Leu Ala Pro Gly Glu Leu Thr Ile Ile Leu  
4550 4555 4560

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<212> PRT  
<213> Homo sapiens

<400> 2

Met Lys Val Leu Trp Ala Ala Leu Leu Val Thr Phe Leu Ala Gly Cys  
1 5 10 15

Gln Ala Lys Val Glu Gln Ala Val Glu Thr Glu Pro Glu Pro Glu Leu  
20 25 30

Arg Gln Gln Thr Glu Trp Gln Ser Gly Gln Arg Trp Glu Leu Ala Leu  
35 40 45

Gly Arg Phe Trp Asp Tyr Leu Arg Trp Val Gln Thr Leu Ser Glu Gln  
50 55 60

Val Gln Glu Glu Leu Leu Ser Ser Gln Val Thr Gln Glu Leu Arg Ala  
65 70 75 80

Leu Met Asp Glu Thr Met Lys Glu Leu Lys Ala Tyr Lys Ser Glu Leu  
85 90 95

Glu Glu Gln Leu Thr Pro Val Ala Glu Glu Thr Arg Ala Arg Leu Ser  
100 105 110

Lys Glu Leu Gln Ala Ala Gln Ala Arg Leu Gly Ala Asp Met Glu Asp  
115 120 125

Val Cys Gly Arg Leu Val Gln Tyr Arg Gly Glu Val Gln Ala Met Leu  
130 135 140

Gly Gln Ser Thr Glu Glu Leu Arg Val Arg Leu Ala Ser His Leu Arg  
145 150 155 160

Lys Leu Arg Lys Arg Leu Leu Arg Asp Ala Asp Asp Leu Gln Lys Arg  
165 170 175

Leu Ala Val Tyr Gln Ala Gly Ala Arg Glu Gly Ala Glu Arg Gly Leu  
180 185 190

Ser Ala Ile Arg Glu Arg Leu Gly Pro Leu Val Glu Gln Gly Arg Val  
195 200 205

Arg Ala Ala Thr Val Gly Ser Leu Ala Gly Gln Pro Leu Gln Glu Arg  
210 215 220

Ala Gln Ala Trp Gly Glu Arg Leu Arg Ala Arg Met Glu Glu Met Gly  
225                   230                   235                   240

Ser Arg Thr Arg Asp Arg Leu Asp Glu Val Lys Glu Gln Val Ala Glu  
245                   250                   255

Val Arg Ala Lys Leu Glu Glu Gln Ala Gln Gln Ile Arg Leu Gln Ala  
260                   265                   270

Glu Ala Phe Gln Ala Arg Leu Lys Ser Trp Phe Glu Pro Leu Val Glu  
275                   280                   285

Asp Met Gln Arg Gln Trp Ala Gly Leu Val Glu Lys Val Gln Ala Ala  
290                   295                   300

Val Gly Thr Ser Ala Ala Pro Val Pro Ser Asp Asn His  
305                   310                   315

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<400> 3

Glu Asn Phe Ala Gly Glu Ala Thr Leu Gln Arg  
1                   5                   10